DESIGN OF TUBE FEEDS FOR SURGICAL PATIENTS

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The recognition of the considerable attrition of body protein and fat that may accompany a major illness or injury has interested many workers in the need for supplementary feeding if convalescence is to be rapid and smooth (Moore and Ball, 1952; Blocker *et al.*, 1955; Sutherland, 1955; Fallis and Barron, 1956; Moore, 1959). The unwillingness or inability of the patient to take a large amount of nourishment, particularly of bulky hospital diet, often justifies nasogastric-tube feeding. Occasionally when there is an obstructing lesion in the upper gastro-intestinal tract gastrostomy or jejunostomy is required. Apart from the use of blended whole food (Fallis and Barron, 1956), which, although successful, requires complicated equipment for its preparation, each worker seems to have developed his own formula or, alternatively, has resorted to the prepared commercial supplementary feeds that are available.

Over the years our experience has been that difficulties and complications still ensue from the use of all these mixtures; often the ingredients favoured by one person are difficult to obtain or are no longer manufactured—for example, some of the foods listed in Moore's (1959) account are not available in Britain. Because of these problems, tube feeding is still looked upon with some distrust by medical and nursing staff except in highly specialized units such as those treating patients for burns or head injuries. The need for supplementary nourishment or total feeding in the old, the uncooperative, the unconscious, and the seriously ill or injured is increasing, and we believe that subclinical malnutrition is now one of the most important causes of prolonged convalescence and may often contribute to a fatal outcome in the complicated surgical or medical case. Because of this need we have re-examined the criteria which should govern satisfactory tube feeding and have endeavoured therefrom to design feeds which are a satisfactory compromise of the multiple requirements involved. Our results have led to a considerable simplification of our feeding schedules.

Methods

Standard metabolic techniques were used in all these studies: nitrogen in milk, feeds, and faeces by the Kjeldahl method; sodium and potassium by flame photometry; urine osmolality to the nearest 5 milliosmols/kg. (mOs/kg.) by freezing-point depression (Advanced Osmometer). Body weight was measured by a modification of the scales described by Sutherland (1955) which allows determinations to ± 5 g., stool fats by the method of van de Kamer *et al.* (1949), and blood urea on the autoanalyser.

Standard conversion factors of 4.1, 3.75, and 9.3 cals./g. were used for protein, carbohydrate, and fat respectively; 6.25 g. of protein was taken as equivalent to 1 g. of nitrogen.

Calories and Their Partition

Although the studies of the metabolic response to surgical operations or to injury have confirmed that an increase in metabolic rate with probably selective breakdown of body protein does take place, this is quantitatively not large and rarely adds more than 750–1,000 calories a day to energy expenditure over a period of three to four days. If, however, insufficient calories are available or can be ingested a progressive calorie deficit soon develops and is the reason for the wasting that may be such a feature of prolonged convalescence; it is the need to remake this lost tissue that accounts for the time taken before the patient feels able to return to work. In many instances such a calorie deficit is already present, and, in spite of Moore's (1959) comment on the ability of the starved to march, fight, or withstand injury, may adversely affect the response to an operation.

The need for calories, therefore, is not so much for very high daily intakes as for adequate calories at an early stage after injury or for a satisfactory allowance in preparation for operation. This calorie intake should have enough margin over a basal allowance to make good deficits if these exist. The provision of 3,000 calories for total nourishment and 2,000 calories as a supplement has, in our experience, usually been sufficient to permit steady weight gain which is not the consequence of rapid change of body water and electrolyte. An active 65-kg. (143-lb.) adult will maintain weight on 3,000 calories, although modern dietary standards in this country usually allow considerable luxus consumption above this amount (Davidson *et al.*, 1959). Provision of calories up to but not above this level simplifies the problem as compared with the more extravagant intakes that have been attempted under special circumstances. The feed should be so designed that expansion of calories to a higher plateau is possible to meet the greater calorie needs of the very extensively injured or the severely infected (Moore, 1959).

The partition of calories between nitrogen on the one hand and fat and carbohydrate on the other hand is a matter which has been the subject of considerable dispute. The high-protein feeding so beloved of many ward sisters seems, at least in part, to be a persistence of the myth that a large quantity of dietary protein is inevitably productive of a superior nutritional—and therefore physical—standard. The use of nitrogen by the body for other than energy purposes is to a considerable extent dependent upon the non-nitrogen calorie intake, and if there is not a pre-existing nitrogen deficit excess nitrogen over certain limits is used only as a source of calories. A careful study of these has been made by Calloway and Spector (1954): Fig. 1, drawn from their data, shows that when the total calorie intake is low, nitrogen in the diet fails to prevent negative balance. With reasonable quantities of nitrogen, balance is unlikely to be achieved below 3,000 calories a day total intake, although a spurious positive balance may be attained by raising intake to 24 g. at around 2,000 cals. Adding nitrogen to the diet between 0 and 750 cals/day total intake does not affect the utilization of endogenous nitrogen. However, as Gamble (1947) first demonstrated in his life-raft studies, the negativity of nitrogen balance is reduced by providing non-nitrogen calories within this range; these spare nitrogen which is otherwise broken down for calorie purposes. At 2,000 cals/day 8 g. of nitrogen (50 g. of protein) can be assimilated with a concurrent negative balance of only 2 g./day. At 3,000 calories equilibrium is achieved with 9–10 g. of nitrogen a day.

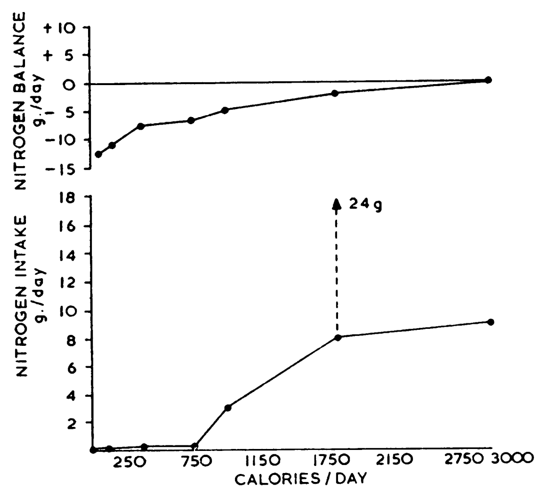

FIG. 1.—Average figures for assimilation and balance of nitrogen in relation to calorie intake, taken from Calloway and Spector (1954). Dotted vertical line at approximately 2,000 calories is theoretical nitrogen intake required for equilibrium (Calloway and Spector, 1954).

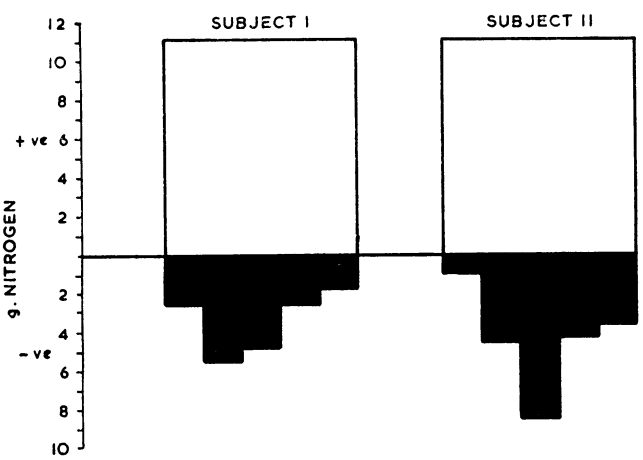

FIG. 2.—Nitrogen balance for two subjects on 2,000 calories and 11 g. nitrogen daily (charting convention from Moore and Ball, 1952: solid areas below baseline indicate negative balance). Note consistent negative balance.

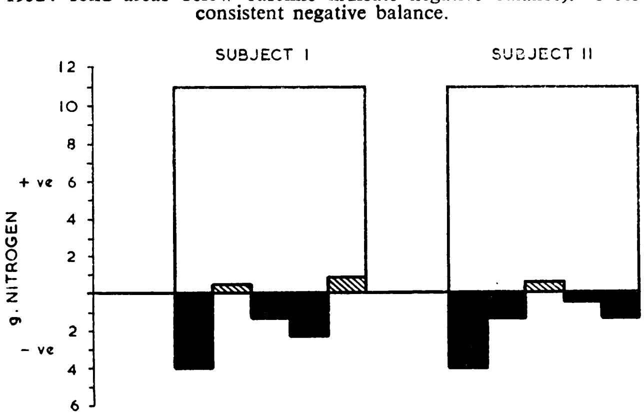

FIG. 3.—Nitrogen balance for two subjects on 3,000 calories and 11 g. nitrogen daily. Note the much smaller negative balance as compared with Fig. 2.

Our own experience is that under conditions of tube feeding the same holds true. Figs 2 and 3 show the nitrogen balance of two healthy adults taking 11 g. of nitrogen and 2,000 or 3,000 calories daily. In the first instance there is a negative balance of up to 8 g. daily, although more usually about 4 g. In the second, that of the higher calorie intake, near balance is seen. The relatively small nitrogen intakes required for nitrogen equilibrium when non-nitrogen calories are adequate does not imply that more nitrogen cannot be utilized when there is need, once these basic requirements have been met. In a study of men on various dietary levels of nitrogen intake during the late recovery phase after extensive trauma and at a time when all wounds were healed but the patients were still much underweight, Forsyth *et al.* (1955) found that a constant proportion of dietary nitrogen (23%) was retained in a range of 16.5–48 g. daily intake—that is, 100–300 g. of protein. Thus when there has been much previous loss of lean tissue, convalescence, at least in theory, will be more rapid if high-protein feeding is used. However, for maintenance such intakes are not required.

There is consequently a need for two types of tube feed for use in total or near total nourishment: one for maintenance, which need contain only relatively small amounts of protein (10–12 g. of nitrogen; 60–75 g. of protein), and one for restitution in the management of the protein-depleted patient. The latter should be able to contain up to 48 g. of nitrogen (300 g. of protein) daily. Protein intakes of this order may be indicated also in circumstances where there is exudate loss from a raw surface such as a burn (Levenson *et al.*, 1952; Sutherland, 1959) or from the colon in ulcerative colitis. For this purpose a pure protein ingredient in the feed is useful because it permits expansion of the nitrogen moiety at will and according to the clinical need (see Table III).

In considering the allowance of protein in a feed it should be remembered that large nitrogen loads lead to a high urinary urea excretion and that this requires urine volume for its excretion. Even at a maximal urinary concentration of 1,100 mOs/kg. urea needs 40 ml. of urine water per gramme. The solute diuresis produced by large quantities of urea may lead to loss of water in excess of intake (*B.M.J.*, 1963). Alternatively, when urine volumes are low, urea clearance is considerably reduced below its maximum value (Möller *et al.*, 1928), the large urea load may be incompletely excreted, and the blood-urea concentration may rise. Wrong and Black (1956) have shown this to be true for one proprietary preparation which provides a considerable excess of nitrogen (24 g. total) at such a low calorie level (2,000 cals/day) that it is extremely improbable that more than a proportion (one-third to one-half) will be retained even if there is a pre-existing protein depletion increasing the avidity of the tissues for nitrogen. This feed is clearly not suitable for maintenance purposes. Although it is usually possible to provide sufficient water to meet the needs of patients on tube feeding, maximal urea clearance is reached only at an inconvenient daily urine volume of 2.5–3 litres; water to provide this volume and replacement for 1–1.5 litres of insensible loss is unquestionably too large a quantity to present to the patient. Large volumes of this kind are also quite unsatisfactory when other liquids such as those draining from a fistula have to be returned.

There are accordingly good reasons for not providing too large a nitrogen intake except in special circumstances. On intakes of 8–11 g. daily with a total water ration of approximately 2.4–2.8 litres, urine volumes are usually in the range 1,000–2,500 ml. and solute concentration 250–900 mOs/kg. Volumes and concentrations of this order demonstrate that a relatively small solute load (500–900 mOs) as compared with 1,100–1,200 mOs on a normal 3,000-calorie diet are being excreted at a convenient submaximal urinary concentration (Figs. 4 and 5). Additional water may, of course, be necessary in a patient suffering from extrarenal losses.

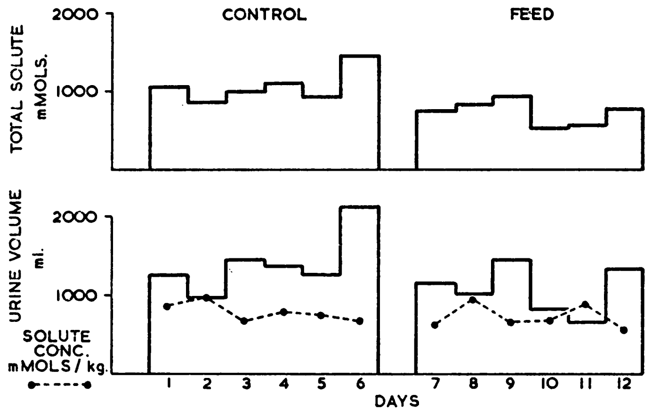

FIG. 4.—Urinary volume, concentration, and total solute excretion for 2,000-calorie feed. Note constancy of urine volume and solute excretion at moderate solute concentrations compared with control. The volume of water supplied was approximately 2.4 litres.

Osmotic Pressure, Carbohydrate, and Electrolyte Content

Having determined the nitrogen content of the feed it would normally be standard dietetic practice to partition the non-nitrogen calories between fat and carbohydrate according to some arbitrary fraction. However, in tube feeding, a further consideration seems to be of great importance—namely, osmotic pressure. Diarrhoea is a not infrequent accompaniment of and reason for dissatisfaction with tube feeding, and, while it may be the result of a number of factors, there seems good reason to suppose, on the basis of the known reaction of the intestine to hypertonic solutions, that a high solute concentration may be one of the more important. Certainly this possibility is a good argument for so designing the feed as to make it as nearly isotonic as possible.

Four or five tube feeds originally recommended were found to have an osmolality in excess of 600 mOs/kg., or twice plasma; the other, designed for intrajejunal use (Moore, (1959), was isotonic (Table I). It is perhaps significant in this context that milk is close to isotonicity. All these arguments apply with greater force where the feed is to be given intrajejunally; diarrhoea is particularly likely to follow this, and it is extremely difficult to achieve weight gain by jejunal feding, as distinct from restoring fluid and electrolyte balance.

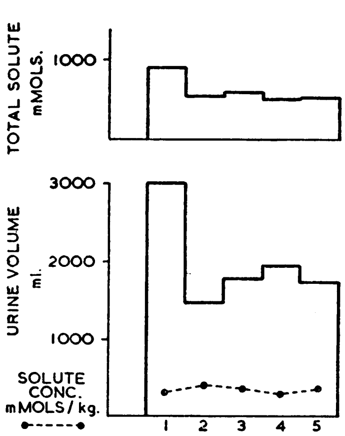

FIG. 5.—Urinary volume, concentration, and total solute excretion for 3,000-calorie feed. Note the low solute concentration of the urine. The volume of water supplied was approximately 2.8 litres.

The components of a feed that contribute to its osmotic pressure are carbohydrate and electrolytes, chiefly sodium, potassium, and chloride. Fat and protein exert negligible effects. Therefore, at any given hypotonic electrolyte level only a certain amount of carbohydrate is admissible to the feed before isotonicity is exceeded. Alternatively, carbohydrate can displace electrolyte to a similar degree. It is common and satisfactory to use lactose as the main source of carbohydrate calories. Compared with glucose or sucrose, lactose has the highest molecular weight, and therefore weight for weight it will have the lowest osmolality. Its solubility factor, on the other hand, is less than that of the other two. Fig. 6 shows its osmolal concentration and calorie contribution within its solubility range. At 150 mOs/kg.—half the concentration of plasma—it supplies 200 cals/l.

TABLE I.—*Recommended Volumes, Calorie Content, and Consequent Osmotic Concentration of Some Common Feeds. Data from Sutherland* (1955), *Dudley et al.* (1958), *Moore* (1959), *and Wilkinson* (1960)

Feed	Volume (ml.)	Total Calories	Osmotic Concentration (mMol/kg.)
Moore (1959) Gastric A ..	1,000	1,570	1,200
,, ,, B ..	1,000	1,970	1,200
,, Jejunal C ..	1,150	1,140	430
,, ,, D ..	1,000	470	300
Sutherland (1955) A ..	700	1,454	860
,, B ..	3,300	3,740	340
Wilkinson (1960) ..	1,900	2,400	680
Complan (Glaxo) ..	3,000	2,000	268
Cow's milk	3,000	2,000	292
2,000-calorie	2,500	2,000	313
3,000- ,, ...	3,000	3,000	325

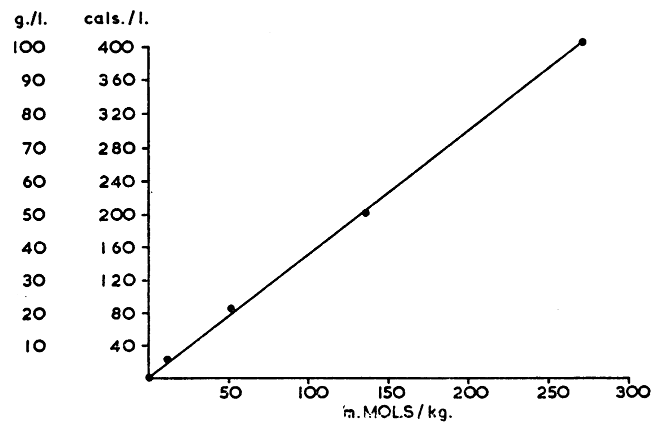

FIG. 6.—Osmotic pressure and calorie contribution of lactose solutions. These figures are experimental findings of the osmolality at various concentrations of lactose.

Therefore even relatively small quantities of carbohydrates will require careful control and partition of electrolyte content if a grossly hypertonic feed is to be avoided. Careless addition of sodium chloride in particular may produce a feed the effect of which differs little from that of a saline cathartic.

Unless there is some condition present for which an additional intake of sodium is required, conservation of this ion by the kidney is such that 30–40 mEq only need be administered each day, although a normal diet in this country may contain three to four times this figure. Fig. 7 shows the attainment of normal sodium equilibrium in two healthy adults taking a tube feed of 3,000 calories and 25 mEq of sodium daily. There is an initial period of negative balance (and consequently of weight loss) before regulatory mechanisms come into play.

Potassium requirements for equilibrium are greater, being in the range of 40–60 mEq/day. The sum of the minimum sodium and potassium needs, together with their accompanying anions, gives a total osmolal concentration of 140–200 mOs. If this is distributed in 2.5–3 litres of feed it will add 45–80 mOs/kg. of feed, according to the amount of diluent and the actual level of ions chosen. This basic information can be used to adjust the osmolality of feeds once the constituents have been specified.

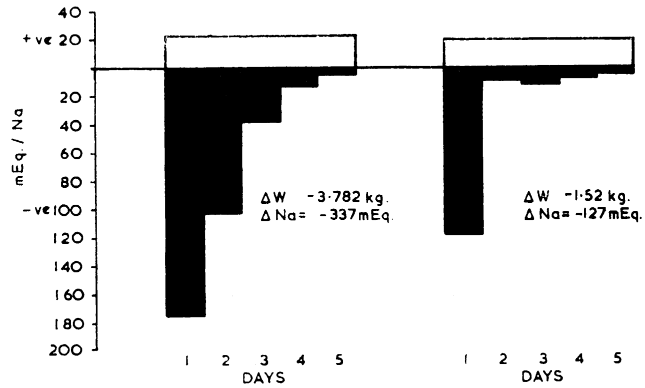

Fig. 7.—Sodium balance of two normal individuals on a 3,000-calorie low-sodium diet. Equilibrium is achieved after an initial period of weight loss.

Fat Content

Given that the protein content is fixed by the ability of the body to utilize nitrogen at any particular calorie level and by the purpose for which the feed is used (maintenance or restitution), and that the carbohydrate content is limited by considerations of osmotic pressure and solubility, the remaining calories must be provided by fat. In the 2,000- and 3,000-calorie feeds under consideration this implies approximately 50% of total calories in each case. Wollaeger *et al.* (1947) and Annegers *et al.* (1948) have shown that this amount of fat should be absorbed without undue difficulty provided there is a normal gastro-intestinal tract. Pimparkar *et al.* (1961) give a mean faecal fat of 4 g. daily, with a range of 2–9 g. Fig. 8 shows faecal-fat excretions for periods of one to three days for normal diets (120–150 g. of fat) and low-fat and high-fat tube feeds, the last containing 50% fine-particle fat. Although faecal-fat excretions show a wide range they reach levels of chemical steatorrhoea in only 8 of 47 instances. Calorie wastage was minimal. On the first day of taking the high-fat feed some subjects complained of diarrhoea, but in all this passed off within 24 hours; the overall effects of these diets, large though their fat content may be, were constipating. Other experiments, using diets of lower fat but higher carbohydrate content and not considered here (Dudley and Masterton, unpublished), showed that additional carbohydrate tended to provoke uncomfortable borborygmi and occasional diarrhoea.

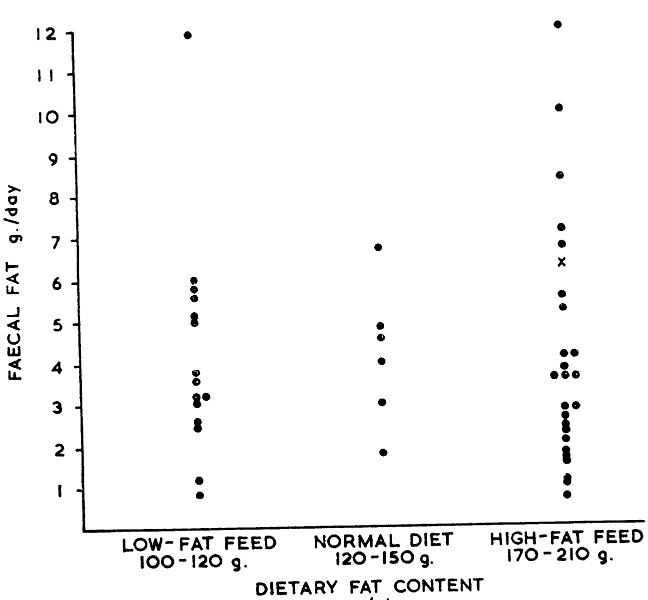

Fig. 8.—Data for faecal-fat excretions of eight subjects on three diets (see text). In right-hand column × is a patient with a transverse colostomy.

These findings of a low faecal-fat loss in spite of large intakes are in accord with the previous studies on sledging rations (Masterton *et al.*, 1957), which also contain high levels of fat (50–60% of total calories). A fat content of 50% of total calories is therefore permissible, although it remains to be shown if this can be successfully introduced as a jejunal, as distinct from a gastric, feed.

Palatability and Constituents

Palatability is an important consideration: first, to avoid an unpleasant regurgitant taste in the mouth in patients fed by tube; secondly, to allow the same formula to be used for oral supplements or a total oral feed in those who can ingest liquids only. For the latter reason it is wise to base the feed on fresh, powdered, or tinned milk, which most people can tolerate, if not enjoy. Crude protein preparations should be avoided and a fine suspension—for example, "casilan"—should be used. Lactose is a satisfactory carbohydrate because it is not intolerably sweet. Small-particle fat emulsion ("prosparol") is virtually tasteless.

The use of such simple ingredients reduces the effort of preparation to a minimum and so removes one of the chief objections to the use of tube-feeding techniques. The composition of the two feeds and the instructions for their use are shown in Tables II and III. They are mixed in a blender, kept cool in a refrigerator, and administered either by drip or using the metering pump previously described (Anderson *et al.*, 1961). Feeds prepared in this manner have a flat but not unpleasant flavour and, particularly if chilled, can provide total calories for many days by mouth,

Table II.—*2,000-Calorie Feed for Full Nourishment in Children or Partial Nourishment in Adults*

Ingredient	Quantity	Protein (g.)	Fat (g.)	Carbohydrate (g.)	Calories
Cow's milk	2,000 ml.	68	74	96	1,320
50% fat emulsion	100 ,,	—	50	—	465
Lactose	60 g.	—	—	63*	236
Water	400 ml.	—	—	—	—
Total		68	124	159	2,021

Weight of feed = 2,617 g. Volume of feed = 2,500 ml. Water content = 2,400 ml. (approx.). Sodium content = 50 mEq. Potassium content = 80 mEq.
* Calculated as monosaccharide.

Table III.—*3,000-Calorie Feed for Full Nourishment*

Ingredient	Quantity	Protein (g.)	Fat (g.)	Carbohydrate (g.)	Calories
Cow's milk	1,000 ml.	34	37	48	660
50% fat emulsion	270 ,,	—	135	—	1,256
Lactose	250 g.	—	—	262*	983
Milk protein	35 ,,	35	—	—	144
Water	1,700 ml.	—	—	—	—
Total		69	172	310	3,043

Weight of feed = 3,273 g. Volume of feed = 2,970 ml. Water content = 2,800 ml. (approx.). Sodium content = 25 mEq. Potassium content = 40 mEq. To increase protein intake to 100 g./day add 30 g. milk protein. To increase protein intake to 200 g./day add 130 g. milk protein. To increase protein intake to 300 g./day add 230 g. milk protein.
See Table IV for additional electrolyte content.
* Calculated as monosaccharide.

even in volunteers. We have not found it useful, either in ourselves or in our patients, to attempt to disguise the feeds. Enthusiasm on the part of the staff is nearly always enough to enable a tube or oral supplement of this kind to be consumed provided it does not produce side-effects such as gastric distension, borborygmi, or diarrhoea. If needed, additional sodium and/or potassium may be added to the feed, thus adjusting the electrolyte content to the needs of the individual patient. Table IV gives instructions for varying the electrolyte content of the 3,000-calorie 3-litre feed. It is to be noted that progressive hypertonicity

TABLE IV.—*Effect of Adding Potassium, as Potassium Chloride, or Sodium, as sodium chloride, to Basic* 3,000-*Calorie Feed*

Potassium			Sodium		
Na (mEq)	K (mEq)	Osmolality (mMol/kg.)	Na (mEq)	K (mEq)	Osmolality (mMol/kg.)
25 (0)	40 (0)	325	25 (0)	40 (0)	325
25 (0)	80 (3)	350	50 (1·5)	40 (0)	340
25 (0)	100 (4·5)	360	100 (4·4)	40 (0)	370
			150 (7·3)	40 (0)	400

Figures in parentheses are the approximate weights in grammes of potassium or sodium chloride which must be added to produce the required daily ration of milliequivalents.
Note the corresponding rise in osmolal concentration.

results and if large additions of electrolyte are needed the volume of the feed should, if possible, be increased.

In clinical practice we have not yet encountered diarrhoea although our experience of intrajejunal feeding is still small. These feeds have in our hands proved their worth and we are using them with increasing frequency in the management of our patients. The cost of each 1,000-calorie unit is a little less than half a crown.

Summary

The characteristics of tube feeds that can also be used by mouth have been re-examined. The most important single factor in a feed, whether it be used as a supplement or for total feeding, is that it should contain adequate calories. High protein intakes without sufficient total calories will not lead to positive nitrogen balance and are not recommended as a basis of tube feeds. In fact, a high protein content can be harmful, since it will produce a solute diuresis due to increased urea production, and in the absence of a high fluid intake this diuresis leads to loss of water in excess of intake. It is stressed that, in addition to calorie content, tube feeds should be sufficiently palatable to be taken by mouth and to prevent any regurgitant taste even when given by tube. The electrolyte and osmolal concentrations of feeds must be carefully controlled, as a lack of attention to these may lead to diarrhoea and relative water deficiency as well as to serum electrolyte imbalance. The use of fine-particle fat emulsion as the major source of calories is advised, since a feed can then be made with a high calorie value but relatively low volume. A series of recommendations are made to facilitate ease of preparation and administration and to increase the flexibility and efficiency of liquid feeding.

One of us (H. A. F. D.) is in receipt of a personal grant from the Medical Research Council. We could not have carried out these studies without the unfailing help of the chief pharmacist Mr. H. N. F. Kinniburgh, Aberdeen General Hospitals Group, whose department weighed many samples of constituents during these trials. Dr. J. Crooks and, more recently, Professor S. C. Frazer have kindly carried out the faecal-fat estimations. We thank Drs. Calloway and Spector and the *American Journal of Clinical Nutrition* for permission to draw Fig. 1.

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TWO CASES OF UNTOWARD REACTION AFTER "ILOSONE"

BY

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The antibiotic "ilosone" (propionyl erythromycin lauryl sulphate or, as it is now called, erythromycin estolate) was first introduced in September, 1958. Since then more than twenty million "courses" have been dispensed, according to prescription surveys conducted by the manufacturers (Dolman, 1963).

During the past two years 59 cases of hepatitis following the use of this drug have been reported to the manufacturers (Dolman, 1963). The exact nature of the disease in some of these reports has been questioned (Dolman, 1963). But 20 cases which have been described in detail (Robinson, 1961, 1962a; Kohlstaedt, 1961; Johnson and Hall, 1961; Havens, 1962; Masel, 1962; Reed and Ritchie, 1962; Riley, 1962; Gilbert, 1962) all presented a syndrome suggestive of cholestatic hepatitis, and most of them developed jaundice. In only two cases was the liver biopsied (Johnson and Hall, 1961; Robinson, 1962a), but in both cases the jaundice had subsided prior to biopsy.

This communication reports two cases of untoward reaction that occurred after the administration of ilosone. In one case a liver biopsy was done while jaundice was present.

Case 1

A man aged 25 was admitted to Wakari Hospital, Dunedin, on September 17, 1962, with a history of jaundice of seven weeks' duration.

In April, 1962, boils had developed on his right arm, for which he was given one 250-mg. capsule of ilosone q.i.d. for